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## REMARKS

This paper responds to the Office Action mailed April 13, 2006. Claims 1-8, 15-20, and 55-86 were pending and claims 1-8, 15-20, and 55-72 were under consideration in connection with the present application. No claims are amended, cancelled, or presented for consideration with this paper. Accordingly, claims 1-8, 15-20, and 55-86 remain pending and claims 1-8, 15-20, and 55-72 remain under consideration.

### I. Restriction

Claims 73-86 stand withdrawn as directed to a non-elected invention and relate to methods for modulating conditions or disorders associated with metabolic or inflammatory disorders. Applicants respectfully remind the PTO that claims 73-86 are method claims that recite all the limitations of the compounds encompassed by, for example, claim 1. As such, Applicants respectfully submit that withdrawn method claims claims 73-86 should be rejoined after the compound claims presently under examination are deemed allowable by the PTO. *See* M.P.E.P. § 821.04(b).

### II. The Rejection of Claims 1-8, 15-20, and 55-72 as Failing to Comply with the Enablement Requirement of 35 U.S.C. § 112, First Paragraph Should be Withdrawn

Claims 1-8, 15-20, and 55-72 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In particular, the PTO argues that the instant specification does not enable one skilled in the art to make and/or use the claimed compounds where X is other than $-S(O)_k-$, -O-, -C(O)-, or $-CH_2-$. Applicants respectfully traverse.

#### A. The Legal Standard

To satisfy 35 U.S.C. § 112, first paragraph, a specification must, *inter alia*, describe a claimed invention sufficiently to enable one of ordinary skill in the art to practice the invention without undue experimentation. *See In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The multi-factor test summarized by the Federal Circuit in *Wands* forms the basis for an inquiry into whether an amount of experimentation is undue.

The *Wands* factors include (1) the quantity of experimentation necessary, (2) the amount of guidance provided, (3) the presence or absence of working examples, (4) the nature of the

invention, (5), the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *See id.* The test for determining whether experimentation is undue is "not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine or the specification provides a reasonable amount of guidance with respect to ... the experimentation." *See Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (1982).

Finally, the PTO must establish a *prima facie* case of non-enablement in order to properly reject a claim on that basis. "When rejecting a claim under the enablement requirement of § 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention in the specification of the application..." *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). The PTO's *prima facie* case should address each of the *Wands* factors since "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the [*Wands*] factors while ignoring one or more of the others." *See* MPEP § 2164.01(a), citing *Wands* at 1407.

**B. Any Experimentation Required to Make and Use the Entire Scope of the Claimed Compounds would be Routine**

At the outset, Applicants respectfully submit that the PTO has failed to make a *prima facie* case of non-enablement of the claims as the PTO has addressed only one of the *Wands* factors, the presence or absence of working examples. Consideration of each of the *Wands* factors demonstrates that the entire scope of the claimed subject matter is in fact fully enabled by the application as filed.

1. *Only Minor Experimentation Would Be Required to Make and Use the Claimed Compounds*

First, Applicants respectfully submit that only minor experimentation would be required to make and/or use compounds where X is other than $-S(O)_k-$, -O-, -C(O)-, or $-CH_2-$. In particular, synthesis of compounds of the invention where X is other than $-S(O)_k-$, -O-, -C(O)-, or $-CH_2-$ can be accomplished using techniques routine to those skilled in the art as guided by the general synthetic scheme presented in the specification at page 22, line 32 to page 24, line 4. Moreover, this synthesis is guided by the more than 350 synthetic reactions specifically

exemplified in the instant application, at least some of which exemplify synthesis of compounds where X is other than -$S(O)_k$-, -O-, -C(O)-, or -$CH_2$-. *See, e.g.*, Examples 75 and 209-216, where X is -$N(R^{11})$-. As such, Applicants respectfully submit that only minor experimentation would be required to make compounds where X is other than -$S(O)_k$-, -O-, -C(O)-, or -$CH_2$-.

Similarly, only minor experimentation would be required to use compounds where X is other than -$S(O)_k$-, -O-, -C(O)-, or -$CH_2$-. Applicants have provided a standard assay that can be routinely used to determine whether compounds within the scope of, for example, claim 1 have substantial PPARγ modulatory activity and/or anti-diabetic efficacy. *See* Examples 373 and 374 at pages 198-200 of the instant application. These assays can be routinely used to confirm that compounds where X is other than -$S(O)_k$-, -O-, -C(O)-, or -$CH_2$- in fact have PPARγ modulatory activity and/or anti-diabetic efficacy. Applicants respectfully remind the PTO that "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *See Wands*, 8 U.S.P.Q.2d at 1404, citing *In re Angstadt*, 190 U.S.P.Q. 214, 217-9 (C.C.P.A. 1976). In view of the substantial guidance provided in the instant application for synthesis and testing of the instantly claimed compunds where X is other than -$S(O)_k$-, -O-, -C(O)-, or -$CH_2$-, Applicants respectfully submit that any expermination required to use the claimed compounds is routine rather than undue.

2. *The Instant Application Provides Substantial Guidance*

As discussed extensively immediately above, the present application provides substantial guidance to enable the skilled artisan to make and use the claimed compounds. Both the general synthetic scheme and the numerous working examples provided as described above provide sufficient guidance for the skilled artisan to make compounds as presently claimed where X is other than -$S(O)_k$-, -O-, -C(O)-, or -$CH_2$-. Similarly, PPARγ modulatory activity and/or anti-diabetic efficacy for such compounds can be routinely determined by the skilled artisan by using the assays set forth in the instant application. Accordingly, this *Wands* factor also supports the conclusion that the full scope of the claims under examination are enabled.

3. *The Instant Application Contains Numerous Working Examples*

As discussed above, the present application contains more than 350 working examples. As noted above, at least some of these working examples set forth compounds where X is -

$N(R^{11})$-, though these are compounds where $Ar^1$ is a moiety other than phenyl or naphthyl. Nonetheless, Applicants respectfully submit that the skilled artisan could use these working examples to guide the synthesis of compounds where $Ar^1$ is substituted or unsubstituted phenyl or naphthyl having X other than $-S(O)_k-$, -O-, -C(O)-, or $-CH_2-$. As such, Applicants respectfully submit that this *Wands* factor supports the conclusion that the instant claims are fully enabled by the present application.

4. *The Prior Art is Advanced*

In addition, the advanced state of the prior art supports enablement of the entire scope of the presently claimed compounds. In particular, the art provides innumerable synthetic schemes and prior art compounds as disclosed in the specification of the instant application that permit the skilled artisan to synthesize compounds where X is other than $-S(O)_k-$, -O-, -C(O)-, or $-CH_2-$. For example, the standard synthetic schemes presented in Hoffman, Organic Syntheses Collective Volume VII (as well as the remaining volumes of this treatise), referenced at page 22 of the instant specification, and as guided by the disclosure of the present application, can be used to make the compounds.

Similarly, the prior art provides additional guidance for testing PPARγ modulatory activity and/or anti-diabetic efficacy. The instant specification at page 24 references two papers, Jiang *et al.*, 1998, *Nature* 391:82-86 and Lehmann *et al.*, 1995, *J. Biol. Chem.* 270:12953-6, that describe assays for assessing PPARγ activity. Further, the specification at page 199 references Shibata *et al.*, 1999, *Eur. J. Pharm.* 364:211-9, which provides an assay that can be used to assess anti-diabetic activity in a mouse model. The prior art therefore provides extensive guidance for making and using the entire scope of the claimed compounds, and this *Wands* factor thus further supports the conclusion of enablement.

5. *The Art is Relatively Predictable*

Further, the art relevant to the enablement of the claimed compounds where X is other than $-S(O)_k-$, -O-, -C(O)-, or $-CH_2$ is relatively predictable and suggests that the instant claims are enabled. While it may not be predicatable whether any *particular* compound within the scope of the presently claimed genus has PPARγ modulatory activity and/or anti-diabetic efficacy, one skilled in the art can predictably make such compounds and test such compounds for the desired activity as extensively discussed above. Thus, notwithstanding the inability to

predict whether an individual compound has PPARγ modulatory activity and/or anti-diabetic efficacy, the skilled artisan can predictably make and test the claimed compounds for such activity. This *Wands* factor therefore supports the conclusion that the instant claims are fully enabled.

6. *The Claims are Not Overbroad*

Finally, Applicants respectfully submit that the claims are not overbroad. As extensively discussed above, one skilled in the art can routinely make and test the entire scope of the presently claimed genus of compounds for PPARγ modulatory activity and/or anti-diabetic efficacy as guided by the disclosure of the specification as filed. As such, Applicants respectfully submit that claims 1-8, 15-20, and 55-72 are fully enabled by the application as filed. Therefore, Applicants respectfully request that the rejection of such claims under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement, be withdrawn.

## III. The Rejection of Claims 1-8, 15-20, and 55-72 under the Judicially-Created Doctrine of Obviousness-Type Double Patenting Should be Withdrawn

Claims 1-8, 15-20, and 55-72 stand rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly obvious variants of claims 1-33 of U.S. Patent No. 6,620,827 ("the '827 patent").

In response, Applicants respectfully submit that no claim of the '827 patent provides motivation to select the specific subgenus of compounds recited by 1-8, 15-20, and 55-72.[1] As such, the ordinarily-skilled artisan would not regard the subject matter of claims 1-8, 15-20, and 55-72 as obvious variants of any claim of the '827 patent.

### A. The Legal Standard

Under the judicially-created doctrine of obviousness-type double patenting, a claim must be patentably distinct from a *claim* of an already issued patent or pending application. *See General Food Corp. v. Studiengesellshaft Kohle mbH*, 23 U.S.P.Q.2d 1839 (Fed. Cir. 1992; emphasis added). If the claim at issue defines more than an obvious variation of the patented or

[1] Applicants note that claims 1-8, 15-20, and 55-62 relate to a particular genus of compounds, while claims 63-72 relate to compositions comprising such compounds. Thus, the compositions of claims 63-72 recite the genus of compounds recited by claims 1-8, 15-20, and 55-62, and thus Applicants address claims 1-8, 15-20, and 55-72 together.

pending claim, it is patentably distinct and rejection of the claim under the doctrine of obviousness-type double patenting is improper. *Id.*

To establish a proper obviousness-type double patenting rejection, the Examiner must show that the claim at issue is a "mere variation" of the patented or pending claim that "would have been obvious to those of ordinary skill in the relevant art." *See In re Kaplan*, 229 U.S.P.Q. 678, 683 (Fed. Cir. 1986). In the analysis, the "patent disclosure may not be used as prior art;" instead, the Examiner must focus on the "subject matter that *has been protected*, not...something one may find to be disclosed by reading them" or the specification. *See General Food Corp.*, 23 U.S.P.Q.2d at 1846, quoting *In re Vogel*, 164 U.S.P.Q. 619, 622 (C.C.P.A. 1970) and *In re Boylan*, 157 U.S.P.Q. 370, 371 (C.C.P.A. 1968).

Moreover, a proper obviousness-type double patenting analysis parallels the obviousness analysis performed under 35 U.S.C. § 103(a). *See In re Braat*, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991) and M.P.E.P. § 804. Thus, arguments showing non-obviousness under 35 U.S.C. 103(a) may be made to show that a claim is not an obvious variant of a patented or pending claim. For example, Applicants may show that the claims at issue are not obvious variants of the patented claims by showing that such claims are not *prima facie* obvious variants of the patented claims. One way Applicants may show such non-obviousness is to show that the patented claims define a genus that does not suggest the species or subgenus recited by the claims at issue. *See In re Baird*, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994).

**B. No Claim of the '648 Patent Suggests Selection of the Subgenus Recited by Claims 39-76 and 80-83**

The PTO argues that "[t]he claims of the ['827] patent are fully encompassed by the instant claims." [Office Action, p. 4]. As discussed further below, Applicant respectfully disagrees. Moreover, none of the claims of the '827 patent suggest the compounds recited by Claims 1-8, 15-20 and 55-72, as none of the '827 patent's claims provides the specific motivation needed to select the particular substituents recited by Claims 1-8, 15-20 and 55-72.

The '827 patent's claims do not encompass all of the subject matter of Claims 1-8, 15-20 and 55-72. For example, in the present claims, $R^3$ can be halogen, cyano, nitro or $(C_1$-$C_8)$alkoxy. In contrast, none of the '827 patent's claims allow $R^3$ to be any substituent other than hydrogen.

Accordingly, the instantly claimed compounds are not in fact encompassed by the claims of the '827 patent.

In addition, Applicants respectfully remind the PTO that the specification of the '827 patent cannot be used to construct the obviousness-type double patenting rejection. Rather, only the *claims* of the '827 patent can be used in this analysis. The '827 patent's claims neither recite possible substituents at the position corresponding to $R^3$ of the instant claims nor provide any motivation to select the particular substituents necessary to construct the particular subgenus recited by the instant claims.

In view of this absence of suggestion or motivation, the PTO cannot establish that claims 1-8, 15-20 and 55-72 are *prima facie* obvious variants of the claims of the '827 patent. As such, Applicants respectfully request that the rejection of claims 1-8, 15-20 and 55-72 as obvious variants of claims 1-33 of the '827 patent be withdrawn.

## IV. The Rejection of Claims 1-8, 15-20 and 55-72 as Anticipated under 35 U.S.C. § 102(e) Should be Withdrawn

Claims 1-8, 15-20 and 55-72 stand rejected as anticipated under 35 U.S.C. § 102(e) by the '827 patent. In response, Applicants respectfully submit that the '827 patent does not disclose a single compound within the scope of the genus defined by claim 1 of the instant application. As such, Applicants respectfully submit that the rejection of claims 1-8, 15-20 and 55-72 should be withdrawn.

### A. The Legal Standard

The standard governing anticipation under 35 U.S.C. § 102 requires strict identity. *See* M.P.E.P. § 2131. Thus, "for a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *See In re Bond*, 15 U.S.P.Q.2d 1566 (Fed. Cir., 1990). Anticipation is not shown even when the differences between the claims and the cited reference are allegedly "insubstantial" and any missing elements could be supplied by the knowledge of one skilled in the art. *See Structural Rubber Prod. Co. v. Park Rubber Co.*, 223 U.S.P.Q. 1264 (Fed. Cir., 1984). Furthermore, in *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 U.S.P.Q. 253 (Fed. Cir., 1985), the Federal Circuit explained that even if the prior art teaches "substantially the same thing" as the

claimed invention, the reference still cannot anticipate the invention. Thus, a cited reference must describe each and every claim limitation in order to anticipate the invention as claimed.



**B. The '827 Patent Does Not Teach Each and Every Element of the Invention of Claims 1-8, 15-20 and 55-72**

Claim 1 as presently pending defines a genus of compounds wherein, *inter alia*, $R^3$ is selected from the group consisting of halogen, cyano, nitro, and ($C_1$- $C_8$)alkoxy. No generic or specific compound disclosed by the '827 patent comprises a halogen, cyano, nitro, and ($C_1$-$C_8$)alkoxy attached to an appropriate aromatic ring as recited by claim 1. As such, the '827 patent does not teach each and every element recited by claim 1, and therefore cannot anticipate this claim. As the remainder of claims 2-8, 15-20, and 55-72 either depend from or incorporate all the limitations of claim 1, the '827 patent cannot anticpate any of the presently pending claims. Accordingly, Applicants respectfully request that the rejection of claims 1-8, 15-20, and 55-72 as anticipated under 35 U.S.C. § 102(e) by the '827 patent be withdrawn.

## CONCLUSION

In light of the above amendments and remarks, Applicants respectfully request that the Examiner reconsider this application with a view towards allowance.

Applicants believe that no fee is due in connection with this response beyond the fees associated with the Petition for Extension of Time. Should an additional fee be required, the Commissioner is hereby authorized to charge any such required fee(s) to Deposit Account No. 50-0487, referencing order number T99-008-3. A copy of this sheet is enclosed for such purpose.

Respectfully submitted,

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